K072547

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510(k) Summary

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Idaho Technology Inc. JBAIDS Tularemia Detection Kit

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

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Date Prepared: September 6, 2007

Device Name: Trade Name: JBAIDS Tularemia Detection Kit

Common Name:

Real-time PCR amplification and detection system for targeted *Francisella tularensis* DNA sequences

Classification Name:

Reagent Kit: *F. tularensis* DNA Reagents (Unclassified)

Device Description: The Joint Biological Agent Identification and Diagnostic System (JBAIDS) Tularemia Detection Kit is a real-time polymerase chain reaction (PCR) reagent kit, which, when used with the JBAIDS instrument and software, allows the qualitative in vitro diagnostic (IVD) detection of a target DNA sequence within the pathogenic bacterium, *Francisella tularensis*, the causative agent of tularemia. Key components of the kit include oligonucleotide primers and a fluorescent-labeled target assay probe that specifically detects *F. tularensis* DNA. The kit is designed for use with the JBAIDS instrument, a portable thermocycler and real-time fluorimeter that performs PCR in glass capillaries.

Before testing, samples are purified using Idaho Technology's 1-2-3™ Sample Purification Kits (or validated equivalent). The resulting purified sample is added to an Unknown reagent vial and an Inhibition Control reagent vial, along with reconstitution buffer. When the organism is present, a fragment of *F. tularensis* DNA is amplified. The amplicon is detected by fluorescence using a specific hydrolysis probe. The hydrolysis probe contains a short oligonucleotide that hybridizes to an internal sequence of the amplified fragment during the annealing phase of the PCR cycle. This probe has the 5' and 3' ends labeled with a reporter dye and a quenching dye, respectively. When the probe hybridizes to the specific DNA target, the Taq polymerase enzyme replicating the target-specific DNA

hydrolyzes the probe, separating the two fluorophores and allowing the reporter dye to fluoresce.

The JBAIDS instrument measures the level of fluorescence from each unknown sample and control. JBAIDS Software analyzes the fluorescence amplification curves and reports results as positive, negative, inhibited, or uncertain. A failure of the Positive or Negative Control will result in the entire run being called invalid. Failure of the Inhibition Control yields an inhibited result when the associated sample has a negative result for the target assay and requires retesting of that sample.

Intended Use: The Joint Biological Agent Identification and Diagnostic System (JBAIDS) Tularemia Detection Kit is a real-time polymerase chain reaction (PCR) test system intended for the qualitative *in vitro* diagnostic (IVD) detection of target DNA sequences of *Francisella tularensis*. The system can be used to test human whole blood collected in sodium citrate or sputum collected aseptically from individuals greater than 18 years of age suspected of having tularemia. In addition, positive blood cultures and colonies may be tested. This assay is intended to aid in diagnosis of individuals presenting with signs and symptoms of pneumonic or typhoidal tularemia. It is not intended to aid in the diagnosis of glandular, ulceroglandular, oculoglandular, or oropharyngeal tularemia.

The JBAIDS Tularemia Detection Kit is run on the JBAIDS instrument using the Diagnostic Wizard. Results are for the presumptive identification of *F. tularensis*, in conjunction with culture and other laboratory tests. The definitive identification of *F. tularensis* from colony growth, liquid blood culture, blood specimens, or sputum specimens requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reports are required.

The diagnosis of tularemia infection must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidence, in addition to the identification of the target either from colonies, blood culture, whole blood specimens, or sputum specimens.

The JBAIDS Tularemia Detection Kit is intended for use by trained clinical laboratory personnel who have received specific training on the use of the JBAIDS Tularemia Detection kit. The level of *F. tularensis* that would be present in blood or sputum of individuals with early systemic or pneumonic infection is unknown. Due to the difficulty in obtaining clinical specimens, the assay was not evaluated with blood or sputum from individuals presenting with signs and symptoms of tularemia and who subsequently developed pneumonic or typhoidal tularemia.

Substantial Equivalence: The JBAIDS Tularemia Detection Kit is substantially equivalent to *F. tularensis* antigens and antiserum used for agglutination tests. The antigens were approved under 510(k) #K952138, and the control antiserum under 510(k) #K952141. The following table compares the JBAIDS Tularemia Detection Kit with this predicate device.

JBAIDS Tularemia Detection Kit vs. *F. tularensis* Antigens.

Element	JBAIDS Tularemia Detection Kit	*F. tularensis* Antigens (#K952138)
Intended Use	Qualitative detection of *F. tularensis* DNA.	Qualitative and semi-quantitative detection of antibodies to *F. tularensis*.
Indications for Use	Identification of *F. tularensis* in individuals suspected of having typhoidal or pneumonic tularemia.	Identification of *F. tularensis* antibodies in individuals suspected of having tularemia.
Technological Principles	Real-time PCR using hydrolysis probes.	Agglutination of antibodies directed at *F. tularensis*.
Assay Target	DNA sequences unique to *F. tularensis*.	Antibodies against *F. tularensis*
Specimen Types	Whole blood (collected in 3.2% sodium citrate), sputum, blood culture or bacterial colonies.	Serum obtained from whole blood.
Instrumentation	JBAIDS instrument (K051713)	None
Time to result	Less than 3 hours	Less than 1 hour for slide-based test. Less than 1 day for tube-based test.
Test Interpretation	Automated test interpretation and report generation.	Subjective interpretation by user.
Physical Properties	Freeze dried reagents with reconstitution buffer and water provided in kit.	Liquid reagents
Storage and Shelf Life	1 year at room temperature (18–28 °C).	Refrigerator temperature (2–8 °C), manufacturer defined expiration date.

The predicate device and the JBAIDS Tularemia Detection Kit have the same intended use. Both provide test results that aid in the diagnosis of tularemia when considered with other clinical and microbiological evidence, both test for *F. tularensis* infection directly from patient specimens, and both provide qualitative test results.

While the basic intended use is the same for the predicate device and the JBAIDS Kit, the technological characteristics are quite different. The *F. tularensis* antigen agglutination test relies on the detection of antibodies to *F. tularensis*, while the JBAIDS Kit detects the organism directly in the patient specimen or from cultures. Because of this, the time for diagnosis differs. Antibodies against *F. tularensis* do not appear for 7 to 14 days after onset of symptoms. In contrast, PCR can detect *F. tularensis* concurrent with, or within a few days of, symptom onset.

While there is no published data on the performance of the predicate device, the sensitivity of other antigen agglutination tests has been described in several studies. In a study by Porsch-Ozcurumez et al., 100% (50/50) of patients diagnosed with tularemia tested positive with agglutination.[1] Bevanger et al. found that 91% (40/44) of patients tested positive with the agglutination test.[2] While the clinical sensitivity of agglutination tests is excellent, sensitivity to all strains of *F. tularensis* is unknown.

These studies also determined the specificity of the antigen agglutination tests. In the study by Porsch-Ozcurumez, 100% (50/50) of serum samples collected from healthy individuals tested negative with the assay.[1] The study by Bevanger also claimed 100% specificity (50/50); however, weak cross-reactivity was noted with *Brucella abortis* and *Yersinia enterocolitica*.[2]

The analytic sensitivity, or inclusivity, of the JBAIDS Tularemia Detection Kit was determined by testing colonies and purified DNA from various subtypes and strains of *F. tularensis*. Of the 27 isolates that were tested, all 27 (100%) were detected.

Analytic specificity, or exclusivity, of the JBAIDS Tularemia Detection Kit was determined by testing colonies of organisms that are phylogenetically related to *F. tularensis* and colonies of unrelated organisms that are likely to be found in clinical samples. Negative results were obtained for 23/24 (95.8%) of the organisms. A weak cross-reaction was seen with the closely related *F. philomiragia* when testing plated colonies, which contain very high levels of organism. *F. philomiragia* is an opportunistic pathogen and is primarily seen in near-drowning patients.[3] To help ensure appropriate diagnosis, information on the weak cross-reactivity and the incidence of *F. philomiragia* infection was added to the package insert.

In addition to analytic studies, a multisite clinical trial was conducted with the JBAIDS Tularemia Detection Kit. Due to the near absence of clinical samples from individuals with a diagnosis of typhoidal or pneumonic tularemia, the clinical trial was limited to an assessment of clinical specificity. Blood and/or sputum samples obtained from subjects with clinical signs and symptoms consistent with systemic tularemia and for whom a blood and/or sputum culture had been ordered were tested for *F. tularensis* using the JBAIDS Tularemia Detection Kit. The results were compared to the gold standard technique of culture. As expected, *F. tularensis* was not identified in any of the blood or sputum cultures. Of the 132 whole blood specimens that gave valid JBAIDS results, all (100%) tested negative. Of the 36 sputum samples that gave valid JBAIDS results, all (100%) were negative.

Because *F. tularensis* is an extremely infectious organism, routine culture of the organism is discouraged as this practice puts laboratory workers at risk of acquiring the disease. In addition, culture lacks clinical sensitivity. In a study comparing the sensitivity of culture and PCR, Johansson et al. found that PCR was positive in 75% (30/40) of serologically confirmed cases of ulceroglandular tularemia, while culture was positive in only 62% (25/40).[4] Johansson also found that PCR could detect cases of tularemia not detected by antibody tests. These published studies demonstrate the clinical utility of PCR assays.

Based on the limited data available for the *F. tularensis* antigen agglutination test, the JBAIDS Tularemia Detection Kit appears to be as safe and effective as the predicate device. The JBAIDS offers advantages over the predicate. First, the JBAIDS software automatically interprets the assay results, reducing the opportunity for user error, and the freeze-dried assay format minimizes assay setup errors. Second, the JBAIDS Kit can more rapidly provide a diagnosis earlier in the course of the infection. The time to results for the JBAIDS Kit is less than three hours, while the antigen agglutination test takes approximately 24 hours. The JBAIDS Kit can be used as soon as symptoms appear, while the antibody agglutination reaction may require that patients be tested at least seven days after showing symptoms for sufficient antibody to be present.

In summary, the JBAIDS assay, while technologically distinct from the predicate, is as safe and effective as the predicate, but could provide a more rapid diagnosis.

References

1. Porsch-Ozcurumez M, Kischel N, Priebe H, Splettstosser W, Finke E, Grunow R. 2004. Comparison of Enzyme-Linked Immunosorbent Assay, Western Blotting, Microagglutination, Indirect Immunofluorescence Assay, and Flow Cytometry for Serological Diagnosis of Tularemia. J. Clin. Diagn. Lab. Immunol. 11:1008-1015.
2. Bevanger L, Maeland J, Naess AI. 1988. Agglutinins and Antibodies to Francisella tularensis Outer Membrane Antigens in the Early Diagnosis of Disease during an Outbreak of Tularemia J. Clin. Microbiol. 26:433-437.
3. Friis-Moller A, Lemming LE, Valerius NH, and Bruun B. 2004. Problems in Identification of Francisella philomiragia Associated with Fatal Bacteremia in a Patient with Chronic Granulomatous Disease. J. Clin. Microbiol. 42:1840-1842.
4. Johansson A, Berglund L, Eriksson U, Goransson I, Wollin R, Forsman M, Tarnvik A, Sjostedt A. 2000. Comparative Analysis of PCR versus Culture for Diagnosis of Ulceroglandular Tularemia. *J. Clin. Microbiol.* 38:22-26.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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DEC 1 9 2007

Re: K072547
Trade/Device Name: JBAIDS Tularemia Detection Kit
Regulation Number: 21 CFR 866.3280
Regulation Name: Francisella tularensis serological reagents
Regulatory Class: Class II
Product Code: OEH
Dated: December 14, 2007
Received: December 17, 2007

Dear Ms Lingenfelter:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
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Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K072547
Device Name: JBAIDS Tularemia Detection Kit

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Prescription Use ___x___ (Part 21 CFR 801 Subpart D) AND/OR Over-the-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE—CONTINUE ON ANOTHER PAGE IF NEEDED)

Freddie M. Poole Concurrence of CDRH, Office of Device Evaluation (ODE)
Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K072547